12/12/03

10/580,261

1-16, 18-22

AMENDMENT TO THE CLAIMS 1-16, 18-22

Please amend claims 2, 4-8, 10, 11, 16 and 18-22, and cancel claim 17, as follows:

1. (Original) A polypeptide, derivative or analogue thereof comprising a tandem repeat of apoE141-149 of SEQ ID No 2 or a truncation thereof, characterised in that at least one Leucine (L) residue of SEQ ID No. 2 is replaced by an amino acid with a side chain comprising at least 4 carbon atoms and at least one Nitrogen atom.

LRKLRKRLL

2. (Currently Amended) The polypeptide, derivative or analogue thereof according to claim 1 wherein the amino acid used to replace the Leucine is selected from the group consisting of Tryptophan (W), Arginine (R), ~~or~~ Lysine (K) and ~~or~~ derivatives thereof.

3. (Original) The polypeptide, derivative or analogue thereof according to claim 2 wherein the amino acid used to replace the Leucine is Tryptophan (W) or a derivative thereof.

4. (Currently Amended) The polypeptide, derivative or analogue thereof according to claim 1 ~~any one of claims 1-3~~ wherein at least two W, R or K substitutions are made.

5. (Currently Amended) The polypeptide, derivative or analogue thereof according to claim 1 ~~any one of claims 1-4~~ wherein at least one further amino acid is replaced with Asparagine (N), Tyrosine (Y), Cysteine (C), Methionine (M), Phenylalanine (F), Isoleucine (I), Glutamine (Q), or Histidine (H) or is deleted.

6. (Currently Amended) The polypeptide, derivative or analogue thereof according to claim 1 ~~any one of claims 1-4~~ with the amino acid sequence:

SP

WRKWRKRWWWRKWRKRWW (SEQ ID No. 3); WRKWRKRWRKWRKR (SEQ ID No. 4); WRKWRKRWWLRKLRKRLL (SEQ ID No. 5); YRKYRKRYYYRKYRKRYY (SEQ ID No. 6); WRKWRKRWWRKWRKRWW (SEQ ID No. 52); WRKWRKRWRKWRKRW (SEQ ID No. 53); WRKWRKRWWFRKWRKRWW (SEQ ID No. 54); WRKWRKRWFFRKWRKRFF (SEQ ID No. 55);

WRKCRKRCWWRKCRKRCW (SEQ ID No. 56); LRKLRKRLLWRKWRKRWW (SEQ ID No. 57); LRKLRKRLLLRKLRKRWW (SEQ ID No. 58); LRKLRKRLLWRKWRKRLL (SEQ ID No. 59); WRKWRKRLLLRKLRKRLL (SEQ ID No. 60); WRKLRKRLLLRKLRKRLL (SEQ ID No. 61); WRKWRKFFFRKWRKRWW (SEQ ID No. 62); WRKWRKRWWFRKFRKRFF (SEQ ID No. 63); RRKRRKRRRRRKRRKRRR (SEQ ID No. 64) ; or KRKKRKRKKKRKKRKRKK (SEQ ID No. 65)

7. (Currently Amended) The polypeptide, derivative or analogue according to claim 1 ~~any preceding claim~~ wherein an amino acid is added to the peptide.

8. (Currently Amended) The polypeptide, derivative or analogue according to claim 7~~8~~ wherein the amino acid is added to the N terminal, C terminal and/or between the ninth ~~9th~~ and tenth ~~10th~~ amino acids of SEQ ID No.2

9. (Original) The polypeptide, derivative or analogue according to claim 8 comprising WRKWRKRWWRWRKWRKRWWR (SEQ ID No. 66).

10. (Currently Amended) The polypeptide, derivative or analogue according to claim 1 ~~any preceding claim~~ which is a peptoid analogue.

11. (Currently Amended) The polypeptide, derivative or analogue according to claim 1 ~~any preceding claim~~ which is a peptide/peptoid hybrid.

12 (Original) A polypeptide, derivative or analogue thereof comprising YRKYRKRYYYRKYRKRYY (SEQ ID No. 6)

13. (Original) A polypeptide, derivative or analogue thereof comprising LRKLRKRLLLRKLRK (SEQ ID No. 7).

14. (Original) A polypeptide, derivative or analogue thereof comprising LRKLRKRLRKLRKR (SEQ ID No. 8).

15. (Original) A polypeptide, derivative or analogue thereof comprising LRKLRKLRKLRKLRKLRK (SEQ ID No. 9).

16. (Currently Amended) A composition, comprising the polypeptide, derivative or analogue according to claim 1 ~~any preceding claim for use as a medicament~~.

Claim 17 (Canceled).

18. (Currently Amended) ~~The use of an~~ An agent adapted to increase ~~capable of increasing~~ the biological activity of the ~~a~~ polypeptide, derivative or analogue according to claim 1 ~~any one of claims 1 - 15 in the manufacture of a medicament for treating viral infections~~.

19. (Currently Amended) A method of preventing and/or treating a viral infection, comprising administering to a subject in need of such treatment a therapeutically effective amount of a polypeptide, derivative or analogue according to claim 1 ~~any preceding claim~~.

20. (Currently Amended) A nucleic acid sequence encoding a polypeptide, derivative or analogue according to claim 1 ~~any of claims 1-15~~.

21. (Currently Amended) A composition, comprising the nucleic acid sequence according to claim 20 ~~for use as a medicament~~.

22. (Currently Amended) A method of preventing and/or treating a viral infection comprising administering to a subject in need of such treatment a therapeutically effective amount of a nucleic acid sequence according to claim 20 ~~or 21~~.

I ~~&~~ 1-16 PEP
II. AGENT (18
III. METH TRTMT (19
IV. NA (20, 21
V METH TRTMT NA (22

Preferred peptides have similar IC_{50} values between viral species. For instance preferred peptides have similar IC_{50} values for inhibiting HSV1, HSV2 and HIV growth.

It will be appreciated that modified amino acids may be substituted into the tandem repeat of $apoE_{141-149}$ with a number of amino acid variants that may be known to those skilled in the art Such peptides will still have antiviral activity provided that the modification does no significantly alter its chemical characteristics. For instance, hydrogens on the side chain amines of R or K may be replaced with methylene groups ($-NH_2 \rightarrow -NH(Me)$ or $-N(Me)_2$).

Preferred peptides according to the first aspect of the invention have the amino acids sequence:

(a) WRKWRKRWWWRKWRKRWW (SEQ ID No. 3). This peptide corresponds to the full length tandem repeat with all Leucines substituted for Tryptophan residues. This peptide is designated GIN 7 when referred to herein.

(b) WRKWRKRWRKWRKR (SEQ ID No. 4). This peptide corresponds to the full length tandem repeat with all Leucines substituted for Tryptophan residues and truncated by the excision of amino acids 9, 10, 17 and 18. This peptide is designated GIN 32 when referred to herein.

(c) WRKWRKRWWLRKLRKRLL (SEQ ID No. 5). This peptide corresponds to the full length tandem repeat with a subset of Leucines substituted for tryptophan residues. This peptide is designated GIN 34 when referred to herein.

(d) WRKWRKRWWRKWRKRWW (SEQ ID No. 52). This peptide corresponds to SEQ ID No. 3 with the W residue at position 9 deleted. This peptide is designated MU 58 when referred to herein.

(e) WRKWRKRWRKWRKRW (SEQ ID No. 53). This peptide corresponds to SEQ ID No. 3 with the W residues at position 9, 10 and 18 deleted. This peptide is designated MU 59 when referred to herein.

(f) WRKWRKRWWFRKWRKRWW (SEQ ID No. 54). This peptide corresponds to SEQ ID No. 3 with the W residue at position 10 substituted with an F. This peptide is designated MU 60 when referred to herein.

(g) WRKWRKRWFFRKWRKRFF (SEQ ID No. 55). This peptide corresponds to SEQ ID No. 3 with the W residues at positions 9, 10, 17 and 18 substituted with F residues. This peptide is designated MU 61 when referred to herein.

(h) WRKCRKRCWWRKCRKRCW (SEQ ID No. 56). This peptide corresponds to SEQ ID No. 3 with the W residues at positions 4, 8, 13 and 17 substituted with C residues. This peptide is designated MU 68 when referred to herein.

(i) LRKLRKRLLWRKWRKRWW (SEQ ID No. 57). This peptide corresponds to SEQ ID No. 2 with the L residues at positions 10, 13, 17 and 18 substituted with W residues. This peptide is designated MU 111 when referred to herein.

(j) LRKLRKRLLLRKLRKRWW (SEQ ID No. 58). This peptide corresponds to SEQ ID No. 2 with the L residues at positions 17 and 18 substituted with W residues. This peptide is designated MU 112 when referred to herein.

(k) LRKLRKRLLWRKWRKRLL (SEQ ID No. 59). This peptide corresponds to SEQ ID No. 2 with the L residues at positions 10 and 13 substituted with W residues. This peptide is designated MU 113 when referred to herein.

(l) WRKWRKRLLLRKLRKRLL (SEQ ID No. 60). This peptide corresponds to SEQ ID No. 2 with the L residues at positions 1 and 4 substituted with W residues. This peptide is designated MU 114 when referred to herein.

(m) WRKLRKRLLLRKLRKRLL (SEQ ID No. 61). This peptide corresponds to SEQ ID No. 2 with the L residue at position 1 substituted with W residues. This peptide is designated MU 115 when referred to herein.

(n) WRKWRKFFFRKWRKRWW (SEQ ID No. 62). This peptide corresponds to SEQ ID No. 3 with the W residues at positions 8, 9 and 10 substituted with F residues and the R residue at position 7 deleted. This peptide is designated MU 116 when referred to herein.

(0) WRKWRKRWWFRKFRKRFF (SEQ ID No. 63). This peptide corresponds to SEQ ID No. 3 with the W residues at positions 10, 13, 17 and 18 substituted with F residues. This peptide is designated MU 117 when referred to herein.

(p) RRKRRKRRRRRKRRKRRR (SEQ ID No. 64). This peptide corresponds to the full length tandem repeat with all Leucines substituted for Arginine (R) residues. This peptide is designated MU 16 when referred to herein.

(q) KRKKRKRKKKRKKRKRKK (SEQ ID No. 65). This peptide corresponds to the full length tandem repeat with all Leucines substituted for Lysine (K) residues. This peptide is designated MU 18 when referred to herein.

The inventor has also appreciated that peptides may be employed according to the invention that comprise more than just a simple dimer tandem repeat of $ApoE_{141-149}$ or a truncation thereof. For instance, peptides comprising a trimer or greater number of repeats may be employed as antiviral agents.

In a further embodiment of the invention, antiviral peptides may be synthesised that comprise a peptide as defined above to which further amino acids have been added. For instance, one, two, three or more amino acids may be added to the C or N terminals of a peptide derived from SEQ ID No. 2. Alternatively the peptide may comprise a tandem repeat of a peptide that is larger than the nine amino acids of SEQ ID No. 1. Such peptides may have amino acids added to the N terminal, C terminal and/or between the 9^{th} and 10^{th} amino acids of SEQ ID No. 2. It is most preferred that the amino acid is added to C terminal and also between the 9^{th} and 10^{th}